Section A
Introduction

30 Introduction to Thyrotoxicosis

Lewis E. Braverman
Robert D. Utiger

Thyrotoxicosis is a common and important thyroid disturbance, it has multiple causes, and its recognition and management are important components of endocrine practice.

We use the term *thyrotoxicosis* to mean the clinical syndrome that results when the circulating concentrations of free thyroxine (T_4) or triiodothyronine (T_3) are increased. The term *hyperthyroidism* is used to mean sustained thyroid hyperfunction associated with sustained increases in thyroid hormone biosynthesis and release from the thyroid gland. Thus, the two terms are not interchangeable. Although many patients with thyrotoxicosis have hyperthyroidism, in other patients thyrotoxicosis is due to processes such as thyroid inflammation or to exogenous thyroid hormone administration.

The pattern of illness in patients with thyrotoxicosis is for the most part independent of its cause. Certain features of the illness, however, often provide clues to the cause of thyrotoxicosis in an individual patient. These features include the duration of thyrotoxicosis, the size and shape of the thyroid gland, and the presence or absence of the extrathyroidal manifestations of Graves' disease. An attempt should be made to determine the cause of thyrotoxicosis in all patients, whether by clinical examination or laboratory testing, since knowledge of the cause determines prognosis and guides therapy.

As shown in Table 30-1, the causes of thyrotoxicosis can be subdivided into those that are associated with hyperthyroidism and those that are not. Each of these disorders is discussed in detail in the following chapters. Among the causes of spontaneously occurring thyrotoxicosis, Graves' disease is undoubtedly the most common. Its frequency as the cause of thyrotoxicosis ranges from about 60% to 90% in different regions of the world; most other cases of thyrotoxicosis are caused by toxic nodular goiter, autonomously functioning thyroid nodules (toxic adenomas), or the several types of thyroiditis.[1,3,6] The other causes of thyrotoxicosis are rare.

Although most patients with thyrotoxicosis usually have overt clinical and biochemical disease, thyrotoxicosis may be subclinical. This is most often defined biochemically as normal serum T_4 and T_3 and decreased thyroid-stimulating hormone (TSH; thyrotropin) concentrations. These patients may or may not have symptoms or signs of thyrotoxicosis; if present, the symptoms usually are mild. The causes of subclinical and overt thyrotoxicosis are similar. Whether and how patients with subclinical thyrotoxicosis should be treated, excluding those in whom it is due to excess exogenous thyroid hormone therapy, is controversial and is discussed further in chapter 91.

The more common clinical manifestations of thyrotoxicosis are listed in Table 30-2, and they are discussed in detail in chapters 38 through 54, which deal with the organ system effects of thyrotoxicosis. None of the clinical manifestations is specific; it is usually the combination of several that brings to mind the possibility of thyrotoxicosis in an individual patient. The frequency and severity of the signs and symptoms vary considerably among patients, so that

Table 30-1. Disorders Associated with Thyrotoxicosis

Type of Thyrotoxicosis	Pathogenic Mechanism
Thyrotoxicosis Associated with Hyperthyroidism*	
States of TSH Excess	
Tumor	Thyrotroph adenoma
Nontumor	Thyrotroph resistance to T_4
Abnormal Thyroid Stimulation	
Graves' disease	TSH receptor antibody
Trophoblastic tumor	Chorionic gonadotropin
Intrinsic Thyroid Autonomy	
Toxic adenoma	Benign tumor
Toxic multinodular goiter	Foci of functional autonomy
Thyroid cancer	Foci of functional autonomy
Thyrotoxicosis Not Associated with Hyperthyroidism†	
Inflammatory disease	
Silent thyroiditis	Release of preformed hormones
Subacute thyroiditis	Release of preformed hormones
Extrathyroidal Source of Hormone	
Exogenous hormone use	Hormone in medication or food
Ectopic thyroid tissue	Dermoid tumor (struma ovarii)

*Thyroid radioactive iodine uptake high.
†Thyroid radioactive iodine uptake low.

Table 30-2. Common Clinical Manifestations of Thyrotoxicosis

Symptoms
- Nervousness
- Fatigue
- Weakness
- Increased perspiration
- Heat intolerance
- Tremor
- Hyperactivity
- Palpitation
- Appetite change (usually increase)
- Weight change (usually loss)
- Menstrual disturbances

General Signs
- Hyperactivity
- Tachycardia or cardiac arrhythmia
- Systolic hypertension
- Warm, moist, smooth skin
- Stare and eyelid retraction
- Tremor
- Hyperreflexia
- Muscle weakness

Signs Associated with Specific Causes of Thyrotoxicosis
- Diffuse, uninodular or nodular goiter
- Thyroid pain and tenderness
- Ophthalmopathy (Graves' disease)
- Localized myxedema (Graves' disease)

some patients may seemingly have only one symptom or sign and others many, and the severity of an individual symptom or sign may vary widely.

Among the factors that determine the manifestations of thyrotoxicosis are the age of the patient[2] and the presence of concomitant disturbances in the function of one or another organ system, so that the impact of thyrotoxicosis is either enhanced or diminished. For example, symptoms of sympathetic activation, such as anxiety and hyperactivity, are less common in older than in younger thyrotoxic patients, whereas those of cardiovascular dysfunction are more common. The correlation between the biochemical severity and the extent of clinical disability from thyrotoxicosis is not a close one.[5]

It is easy to obtain biochemical confirmation of thyrotoxicosis by measurements of serum TSH and direct or indirect measurements of serum free T_4 and T_3 concentrations. In contrast, use of biochemical tests to determine the cause of thyrotoxicosis is less convenient and reliable, but fortunately is not routinely necessary. Finally, although the various antithyroid treatments available effectively ameliorate hyperthyroidism and therefore thyrotoxicosis, and preferences for them vary widely,[4] they are

not ideal because they do not address the fundamental abnormality that causes thyrotoxicosis in most patients.

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Edited by

Lewis E. Braverman, MD
Professor of Medicine, Nuclear Medicine, and Physiology
Director, Division of Endocrinology and Metabolism
Chairman, Department of Nuclear Medicine, University of Massachusetts Medical School, Worcester, Massachusetts

Robert D. Utiger, MD
Clinical Professor of Medicine, Harvard Medical School
Deputy Editor, New England Journal of Medicine, Boston, Massachusetts

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